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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,138	SCHLESSINGER ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 8, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) ~~1-4,7,8,~~*11-13 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,11-13 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 7-8,11-13 and 26 all recite a new combination of claim limitations through dependence upon amended independent claims.
Claims 5-6,9-10 and 14-25 have been canceled.
1. The text of those sections of Title 35, U.S. Code not included in this action can be found

in a prior Office action.

Rejections Withdrawn

1. Claims 1, 3, 5-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-19 of U.S. Patent No. 6,514,981, in light of the amendments of the claims, and Applicant's responses, the rejection is herein withdrawn.
2. Claims 1-5,7 rejected under 35 U.S.C. 102(b) as being anticipated by Sugen, WO96/18738 (Reference cited in Applicant's USPTO-1449).
1. Claims 1, 3 and 7 rejected under 35 U.S.C. 102(e, filing date July 1994) as being anticipated Hirth et al, is herein withdrawn in light of the amendment of clam 1 to recite the phrase "one or more indolinones" which is not taught or disclosed by Hirth et al.

Objections and Rejections Maintained

2. ***Priority*** (Issue remains) Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120. The Specification recites the following sentence. "The present application is related to US Application Serial Number 08/357,642",. The priority not granted should be removed/amended to reflect the specific relationships to which the instant Application has priority.
3. (Maintained) Claims 1-7 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps and for omitting essential elements, such omission amounting to a gap between the elements, is herein maintained, despite the fact that Applicant has amended the claim to recite the term "indolinones" in the preamble and three methods steps. (see responses to arguments below).
4. (Maintained) Claims 8,11-13 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps and for omitting essential elements, such omission amounting to a gap between the elements, is herein maintained despite the fact that the claims have been amended to recite specific types of diseases and three methods steps. See responses to arguments below.

Double Patenting

5. (Maintained) Claim 1 (Method of identifying/screening) of this application is in conflict with claim11 in light of claim 9 of Application No. 10/292,524. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant

is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

6. (Maintained) Claims 1-4, and 7 of this application conflict with claims 16-34 of Application No. US 10/464,805. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

7. (Maintained) Claims 1, 3, 7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-10 and 18 of U.S. Patent No. 6,689,806. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound define as a species of indolinone compound, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating serine protein kinase activity (see '806, claim 15) which is within the definition of PYK2 of the instant Specification (see Instant specification page 2, paragraph 2 "Raf" and "CAK" and "CAD" and page 9, paragraph 5, "phosphorylation of a natural binding partner on tyrosine, threonine or serine residues"// US Pat. 6,689,806, col. 52, lines 64-67 and col. 53, line 12). The instant claims recite the term "assaying" and the allowed claim recites "contacting"; these are analogous terms. The instantly claimed genus of methods is anticipated by the allowed species.

8. (Maintained)Claims 1, 3, 7, 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-8,13-14 of U.S. Patent No. 6,680,335. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound define as a species of indolinone compound defined in claim 1 of US Pat. 6,680,335, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating of serine protein kinase activity (see US Pat. 6,680,335 claim 13-14) which is within the definition of PYK2 of the instant Specification (see Instant specification page 2, paragraph 2 "Raf" and "CAK" and "CAD" and page 9, paragraph 5, "phosphorylation of a natural binding partner on tyrosine, threonine or serine residues"; US Pat. 6,680,335, claim 15). The instantly claimed genus of methods is anticipated by the allowed species.

9. Claims 1-4, 7-8 and 11-13 and 26 are rejected under 35 USC 112, second paragraph for reasons of record and responses set forth below.

10. Claims 8, and 11-13 and new claim 26 under 35 U.S.C. 102(b) as being anticipated by Sugen, WO96/18738 (Reference cited in Applicant's USPTO-1449) is maintained for reasons of record and responses set forth below.

11. Claims 1-4,7 are rejected under 35 U.S.C. 102(e, filing date June 7, 1995) as being anticipated Tang et al (US Pat. 5,880,141), is maintained for reasons of record and responses set forth below.

Response to Arguments

12. Applicant's arguments filed June 8, 2005 have been fully considered but they are not persuasive.

13. The rejection of amended claims 1-4 and 7 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps and for omitting essential elements, such omission amounting to a gap between the elements is traversed on the grounds that:

a. the recited methods steps are defined at pages 5, 6, 8-9 and 32, and based upon the claim amendments the rejection under 25 USC 112, second paragraph is moot.

14. It is the position of the examiner that the:

b. first recited methods step measures the interaction of any PYK2 polypeptide with a natural binding partner. The natural binding partner and PYK2 are defined in the claims to be abnormal, or mutants of the native proteins and therefore encompass natural, native interactions.

c. The second step of amended claim 1 recites the step of "comparing said level to the normal interaction level". Step (b) cannot be carried out because the level determined in the first step (a) is the normal level. No point of comparison is defined by steps (a) and (b) because only a normal interaction level is defined by step (a) and step (b). Comparing the level determined in step (a) with a normal interaction level would not determine any difference in binding through carrying out the comparing step of step (b).

d. The third step of amended claim 1 recites the phrase "identifying indolinones that are able to modulate an interaction between a PYK2 polypeptide and a natural binding partner". No indolinones have been contacted with PYK2, no indolinones have been added to the measuring or comparing steps. Therefore no indolinone compounds can be identified as modulating the interaction of PYK2 and the natural binding partner, as the combination of three reagents has not been positively set forth in the claim.

Despite the fact that the claims have been amended to recite three methods steps, the modulation cannot be determined as no indolinones have been combined with the PYK2 polypeptide and its natural binding partner. While a starting point has now been defined in the claims, modulation cannot be determined in light of the fact that no indolinone has been contacted with the PYK2 polypeptide/natural binding partner complex.

An increase or decrease in the interaction between a PYK2 polypeptide and a natural binding partner also can not be determined based upon the methods step of "identifying indolinones" because no indolinones have been positively added to the reaction mixture of the PYK2 polypeptide and the natural binding partner. No means for identification of any type of interaction, no less modulation, is positively recited in the claims. Essential elements to determine modulation, and methods steps which recite essential steps to determine modulation are missing. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed relative to what is being assayed to determine an interaction, and whether or not

the compound modulates the interaction. See In re Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The newly submitted claim limitations "normal interaction level" lacks antecedent basis in the claims 1-4 and 7 that recites just the term "level". The level recited in paragraph (a.) is not defined to be normal or abnormal or indicative of any disease. The claims are incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01.

15. The rejection of claims 8, 11-13 and 26 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps and for omitting essential elements, such omission amounting to a gap between the elements is traversed on the grounds that claim 8 has been amended to recite three methods steps of measuring, comparing and detecting a change in the interaction as an indication of a connective tissue disease, ulcerative colitis or Crohn's disease.

16. It is the position of the examiner that while the claims now recite three methods steps, one being directed to the measurement of PYK2 binding to the natural binding partner, the PYK2 and the binding partner have not been defined be from an abnormal source, and therefore define a measuring step of just binding between PYK2 and the natural binding partner. The binding could be artificial (laboratory reagents), could be normal binding present under normal conditions, or could be between abnormal levels between reagents; but the claims do not define any specific source for the binding. No sample obtained from a patient that is ill is evaluated, only a reference measurement of PYK2 and its' natural binding partner are measured.

Additionally, the comparison step can not determine any difference in the measured level, because the comparing step is carried out with the normal level of PYK2/natural binding partner interaction, and the level determined in step (a) appears to be a the normal level. A change cannot be determined/measured because no differences in binding would be detected in the methods steps of steps (a) and (b). The change measured need only be *an indication* of the recited diseases, and therefore need not be a diagnostic change. There is lack of antecedent basis for the term "indication" in the recitation of the term "diagnosis" of the preamble. Diagnosis is a measure of the presence or absence of a disease, and an indication is not necessarily diagnostic, but could be a sign of a possible disease being present. Natural variations in PYK2 levels have been determined to vary based upon age of the subject (see Menegon et al abstract cited), and the type of tissue, fluid or cell being evaluated (see Kreutz et al (abstract), increase due to optic nerve crush (abstract P14-23); over expressed in hepatocellular carcinoma (see Fujii et al, J. of Hepatology); Picascia et al (article) PYK2 decreased in prostate cancer). A single indication would not be clearly diagnostic of all three different diseases recited in the claim "connective tissue disease", "ulcerative colitis" and "Crohn's disease". The detecting step still lacks essential elements for carrying out the method of diagnosing any type of connective tissue disease, ulcerative colitis or Crohn's disease. The claims still lack a point of reference for change. The measuring step does not measure PYK2 and natural binding partner in a patient sample obtained from a patient with symptoms of connective tissue disease, ulcerative colitis or Crohns's disease. The measuring step defines the normal level of binding between PYK2 and its' natural binding partner. The claimed methods step only defines an indication, but the preamble requires diagnosis; the recited methods steps do not positively correlate with the recited intended use of the claimed method. Natural changes in kinase levels are not taken into consideration, in detecting a change in the interaction (see Menegon et al abstract that shows based upon age,

the levels of PYK2 differ "Whereas PYK2/CAKbeta expression increased with postnatal age and was maximal in the adult, FAK+ levels were stable. PYK2/CAKbeta mRNAs, detected by in situ hybridization were expressed at low levels in the embryonic brain and became very abundant in the adult forebrain").

The source of the interaction is not defined to be normal or abnormal, therefore the detecting need not be indicative of anything as what is detected does not correlate with anything despite the fact that the preamble and the claims have been amended to recite specific diseases and three methods steps. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

17. The obviousness type double patenting rejection over amended claim 1 (Method of identifying/screening) of this application is in conflict with claim 11 in light of claim 9 of Application No. 10/292,524 is traversed on the grounds that claim 11 is not directed to indolinones.

18. It is the position of the examiner that within the scope of claim 11 are the indolinones recited in claim 9 of Application 10/292,524. Though the method of claim 9 does not define a method of measuring modulation of PYK2 and the natural binding partner, claim 11 sets forth the combination of PYK2 and its natural binding partner and adds a modulating compound, the compounds being screened defined to include the compounds of claim 9. The instantly claimed species of invention is an obvious method within the genus of methods set forth in claim 11 of Application 10/292,524 because Application 10/292,524 defines indolinones to be among the compounds to be identified as modulators of PYK2 and the natural binding partners interactions in pending claim 9 of 10/252,524.

19. The obviousness type double patenting rejection over amended claims 1-4, and 7 of this application conflict with claims 16-34 of Application No. US 10/464,805 is traversed by requesting the rejection be held in abeyance until there is allowable subject matter.

20. The rejection is maintained, as the obviousness type double patenting rejection has not been obviated.

21. The obviousness type double patenting rejection over amended Claims 1, 3, 7 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-10 and 18 of U.S. Patent No. 6,689,806 is traversed on the grounds that the method of claim 1 requires the "measuring an interaction between PYK2 and a natural binding partner" and claim 9-10 are not directed to measuring an interaction.

22. It is the position of the examiner that the method of claim 18 which depends from claims 10 and 9, respectively, measures the modulation of a cellular tyrosine kinases which includes the species PYK2. US Pat. 6,689,806 defines cellular protein kinases to be non-receptor tyrosine kinases, which would include PYK2 which is defined to be a non-receptor tyrosine kinase. The indolinone of US Pat. 6,689,806 is contacted with the kinase, and the natural binding partners of the kinase present in the cell. Modulation of the interaction of the kinase with the natural binding partner and the indolinone would be identified at the cellular level based upon monitoring effects upon the cells. The instantly claimed species of invention is an obvious member of the allowed genus of methods that identifies indolinones that modulate interactions between the kinase, the natural binding partner(s) present in the cell through modulatory effects produced and identified at the cellular level.

23. The obviousness type double patenting rejection of claims 1, 3,7, 8 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-9,13-14 of U.S. Patent No. 6,680,335.

24. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound defined as a species of indolinone compound defined in claim 1 of US Pat. 6,680,335, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating PYK2. The normal level of protein tyrosine kinase is determined through the cellular growth and the measured interaction of the protein tyrosine kinase with the natural binding partner (allowed claim 8) in determined through monitoring changes in the cells, or phosphate concentration (see claims 7-8 or '335) in the presence of an indolinone compound. The US Pat. 6,680,335 discloses modulations with the natural binding partner (see col. 12, lines 15-23) and states that the "invention is therefore

directed to compounds which regulate, modulate and/or inhibit tyrosine kinase signal transduction by affecting the enzymatic activity of the RTKs and/or the non-receptor tyrosine kinases and interfering with the signal transduced by such proteins. More particularly, the present invention is directed to compounds which regulate, modulate and/or inhibit the RTK and/or non-receptor tyrosine kinase mediated signal transduction pathways as a therapeutic approach to cure many kinds of solid tumors, including but not limited to carcinoma, sarcoma, leukemia, erythroblastoma, glioblastoma, meningioma, astrocytoma, melanoma and myoblastoma. Indications may include, but are not limited to brain cancers, bladder cancers, ovarian cancers, gastric cancers, pancreas cancers, colon cancers, blood cancers, lung cancers and bone cancers."

25. The patent further discloses that (see '335, col. 17, lines 64-67 and col. 18, lines 1-8) "The compounds of the present invention are also effective in treating diseases that are related to the PYK-2 protein. This protein, its cellular function, and diseases related to them are set forth in detail in U.S. applications Ser. No. 08/357,642, filed Dec. 15, 1994, by Lev et al., and entitled "PYK2 RELATED PRODUCTS AND METHODS" (Lyon & Lyon Docket No. 209/070), and Ser. No. 08/460,626, filed Jun. 2, 1995, by Lev et al., and entitled "PYK2 RELATED PRODUCTS AND METHODS" (Lyon & Lyon Docket No. 211/121), which are hereby incorporated by reference herein in their entirety, including any drawings."

26. The instantly amended claims set forth a genus of methods that evaluate and detect modulations with indolinones, and the allowed claims are directed to specific species of indolinone recited in claim 1 of the issued patent '335. The instantly claimed methods are an obvious variant of the allowed claims.

27. The rejection of claims 8, and 11-13 and new claim 26 under 35 U.S.C. 102(b) as being anticipated by Sugen, WO96/18738 (Reference cited in Applicant's USPTO-1449) is traversed on the grounds that claim 8 has been amended to recite "a method for diagnosis of a connective

tissue disease, ulcerative colitis or Crohn's disease" and WO96/18738 fails to disclose a method for diagnosis of a connective tissue disease, ulcerative colitis or Crohn's disease.

28. It is the position of the examiner that amended claim 8 recites three methods steps, the steps being:

(**Amended claim 8,** (see WO96' page 23, lines 24-30)):

e. **measuring** the level of interaction between PYK2 polypeptide and a natural binding partner ("measuring or detecting various properties including the level of signal transduction and the level of interaction between PYK2 polypeptide and a NBP"; and the use of "animals", see page 6, line 3; (e.g. PYK2:NBP complexes; see page 72, section XVI, lines 25-36, page 73, lines 1-36)

f. **comparing** said level to the normal interaction level (PYK2 and a natural binding partner complex formation (see page 89, lines 10-37; "abnormal level of interaction "see page 24, lines 4-10) . The presence of abnormality inherently comprises step of *comparing* the level to the normal level, so the abnormal level can be determined. The abnormality being indicative of a change in a signal transduction pathway (see abstract, front page "a disease or condition characterized by an abnormality in a signal transduction pathway") that includes an interaction (see page 16, lines 10-17) between a PYK2 polypeptide and a natural binding partner (NBP) (see page 7, lines 2-27 defines binding partners for PYK2).)

g. **detecting** a change in the interaction of the PYK2 and the natural binding partner is determined (detecting a change in the interaction between PYK2 polypeptide and a natural binding partner, the change being indicative of a disease or disorder (see page 88,

section XIX, lines 33-36 and page 89, paragraph 1, "an abnormal quantity of the complex" is compared with a normal range). The change being an indication of an inflammatory condition associated with inflammatory bowel diseases through evaluation of intestinal cell (see page 25, line 27) and GI-tract cells (see page 25, line 27) , both cells associated with the bowel.)

(Instant claims 11): recites various intended uses of the claimed method, but the method does analyze a sample from any specific source, or correlate the change with presence or absence of the recited diseases, but only measures any level of change in the interaction of PYK2 polypeptide and a natural binding partner. In light of the fact that Sugen does disclose a method that detects an abnormal level of interaction, the reference anticipates the instantly claimed methods as the methods steps claimed are disclosed by Sugen.

(Instant claim 12): wherein the interaction is: PYK2 phosphorylation (see page 7, lines 12-21; page 7, lines 22-30); PYK2 to phosphorylate RAK (a natural binding partner, see page 165, line 16 "promotes" interaction); PYK2 and a natural binding partner complex formation (see page 56, section XI, lines 15-35 and lines 1-13; De-phosphorylation (see page 55, lines 20-33, specifically line 32 "inhibit or decrease the dephosphorylating activity"); Reversible phosphorylation of certain proteins (see page 3, lines 4-5 and 6-36; "and page 7, line 22 "Activated PYK2 phophorylates RAK" and page 7, line 15-16 "PYK2 enzymatic activity is positively regulated by phosphorylation on tyrosine") the disruption of the interaction between RAK and PYK2 would be the result of dephophorylation, as interaction between RAK and PYK2 is contingent upon the presence of phosphate added to RAK. PYK2 de-phosphorylation (see page 25, lines 6-10) Binding of PYK2 to its' natural binding partner is contingent upon

phosphorylation (see page 7, lines 12-21, especially lines 14-15 "PYK2 enzymatic activity is positively regulated by phosphorylation on tyrosine) and (see page 16, lines 3-9 "In preferred embodiments).

(Instant claims 13 and 26) wherein the change is an increase or decrease in said interaction (see page 18, lines 19-20).

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

2. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art≅.

29. The rejection of claims 1-4, and 7 under 35 U.S.C. 102(e, filing date June 7, 1995) as being anticipated Tang et al (US Pat. 5,880,141) as evidenced by Swiss Prot accession number Q14289 is traversed on the grounds that: the '141 patent does not specifically disclose the measuring of an interaction between PYK2 and a natural binding partner.

30. Tang et al discloses the instantly claimed invention directed to a:

(instant claim 1) method of identifying indolinone compounds potentially useful to treat or to prevent disease or disorder through identifying modulators of non-receptor kinase inhibitors (see US Pat. 5,880,141, col. 2, lines 58-63), the method, comprising the step of:

measuring the level of interaction (see Example 6, col. 14, lines 56-60 "any tyrosine kinase") between a PYK2 polypeptide (includes subfamilies of non-receptor protein kinases including the subfamily of kinases of Fak see ('141, col. 2, line 45 ;and Swiss Prot accession number Q14289 as evidence that the Fak family of non-receptor protein kinases inherently includes PYK2)

and a natural binding partner (see col. 4, lines 25-31 and col. 1, lines 24-31 "Binding sites are thereby created for intracellular signal transduction molecules and lead to the formation of complexes with a spectrum cytoplasmic signaling molecules that facilitate the appropriate cellular response"), the measurement being associated with signal transduction phosphorylation (see assaying indolinones, Example 5, sections 5.1-5.6, also see '141, col. 7, lines 47-54 "a compound is subjected to a series of screens to determine the compounds ability to modulate, regulate and/or inhibit cell proliferation. These screens, in the order in which the are conducted, include biochemical assays, cell growth assays and in vivo experiments"; col. 15, lines 4-9)

Comparing said level to the normal interaction with effects associated with kinase inhibition or activation (see Tang et al, col. 15, lines 3-17)

associated with one or more indolinone compounds (see '141, col. 3, lines 10-33)

being evaluated for the ability to modulate the interaction between components of the normal interaction (e.g. Tyrosine kinases are non-receptor-type enzymes and are included within the scope of the instantly claimed invention at Specification page 2, paragraph 3). An anti-phospho-tyrosine antibody is utilized in measuring and identifying changes in kinase activity (see col. 17, lines 15-16 ; col. 15, lines 7-10 "as well as non-receptor tyrosine kinases", and section 6.1.1 "inhibition or activation" "assay to conducted to measure kinase activity"; col. 24, lines 45-49: "maximal phophtyrosine signal is determined by subtracting the value of the negative controls from the positive controls. The percent inhibition of phophotyrosine content for extract-containing well is then calculated after subtraction of the negative controls")

Identifying indolinones (see Tang et al title and Example 5) that are able to modulate an interaction between PYK2 (Fak subfamily member, evidence provided by Swiss Prot accession number Q14289)

polypeptide and a natural binding partner (see col. 3, lines 28- 38 "modulating, regulating and/or inhibiting tyrosine kinase signal transduction").

(Instant claim 2): connective tissue disease (see col. 4, line 36 "arthritis"; col. 8, line 3 "destroy cartilage")

(Instant claim 3): *in vitro* (see col. 3, line 9 "ELISA type assays in microtitre plates")

(Instant claim 4): in vivo (see col. 7, line 54)

(Instant claim 7): inhibition of formation of a complex with a natural binding partner (see brief summary text) "Such a composition is believed to modulate signal transduction by a tyrosine kinase, either by inhibition of catalytic activity, affinity to ATP or ability to interact with a substrate." Kinases are known to evidence phosphorylation activity (see col. 1, line 25).

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Conclusion

31. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

32. Bacon, K et al (2003, abstract) is cited to show increases in PYK2 being affected by bacterial infection by Helicobacter pylori.

33. Fujii, T et al (2004) is cited to show over expression of FAK non-receptor tyrosine kinase in hepatocellular carcinoma (see title and abstract).

34. Kreutz, M et al (2003) is cited to show PYK2 up regulation in optic nerve crush (abstract).

35. Menegon et al (1999, abstract) is cited to show variable expression levels of PYK2 based on developmental age.

36. Picascia, A et al (2002) is cited to show an inversely correlated with degree of malignancy of prostate cancers (abstract narrative).

37. Russell et al (2003, abstract only) is cited to show down regulation of PYK2 after chronic exposure to a psychostimulant and withdrawal.

38. Stanzione et al (2001, abstract) is cited to show a decline in PYK2 expression in prostate cancer progression.

39. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

40. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
August 11, 2005

L. R. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600